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A COMPARISON OF SLEEP PROFILES IN PATIENTS WITH DEMENTIA WITH LEWY BODIES AND ALZHEIMER'S DISEASE

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ABSTRACT

Introduction. Sleep disturbances are common in healthy old age and in dementia syndromes. Polysomnography has demonstrated typical changes in both Alzheimer's disease (AD) and dementia with Lewy bodies (DLB) with AD being characterised by sundowning and sleep apnoea and DLB patients showing more disturbances of movement control during sleep. The technical difficulties associated with EEG sleep recordings mean that polysomnography is not possible out of specialist centres.

Objectives. To use questionnaires to assess the frequency of sleep disturbances in patients with Alzheimer's disease and dementia with Lewy bodies.

Method. The sleep profiles of twenty patients with AD and 17 with DLB were assessed using three questionnaires, one designed to assess night time sleep disturbance, one day time sleepiness and the last carer burden. The sleep questionnaires were repeated in a subgroup after treatment with a cholinesterase inhibitor (rivastigmine).

Results. Level of sleep disturbance in both groups was high. DLB patients had more overall sleep disturbance, more movement disorders whilst asleep and more abnormal day time sleepiness. Treatment with rivastigmine produced a trend towards normalisation of sleep profile in a small number of subjects.

Conclusions. Both groups have extensive sleep problems. The DLB and AD groups have different sleep profiles that are of diagnostic importance and may suggest different treatment strategies. The results are consistent with those found from polysomnographic assessment and suggest that the questionnaires used are sensitive to detect differences previously documented with polysomnography.

KEY WORDS—Alzheimer's disease; dementia with Lewy bodies; sleep; cholinesterase inhibitors

INTRODUCTION

Alzheimer's disease (AD) and dementia with Lewy bodies (DLB) are both common progressive dementing illnesses associated with changes in sleep profile. Sleep disturbance adds to carer burden and may lead to the prescription of additional medication (McGaffigan and Bliwise, 1997). Despite the frequency and severity of sleep disturbance in the elderly, little attention is paid to sleep disturbance in schemes for psychiatric history taking or in the standard textbooks. In a Medline search for the years 1993 to date, only 676 out of 74 098 papers, less than 1%, published with a key word of 'old' or 'elderly', mention sleep in the title or abstract.

In patients with AD the most common sleep behaviours are a tendency to confusion in early evening (sundowning) and wandering at night (Ancoli-Israel *et al*., 1993, 1994). Daytime napping is increased compared to age-matched controls. The degree of sleep disturbance, both assessed by clinical observation and polysomnography, tends to worsen as memory impairment worsens (Pollack, 1997). An accurate description of the changes found in sleep in AD is hampered by the fact that many studies do not differentiate between mild,

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moderate and severe dementia and the diagnosis is often less than rigorous. Sleep apnoea may also be more common in dementia patients than age-matched controls (Bahro *et al*., 1993; Bader *et al*., 1996).

Typical electro-encephalographic changes have been described in AD as showing a relative decrease in the proportion of rapid eye movement (REM) sleep (Ancoli-Israel *et al*., 1994). As REM sleep is generated and maintained by cholinergic activity, this is a predictable consequence of the marked loss of cholinergic neurones. Cortically expressed EEG events such as sleep spindles and K complexes are less frequent in patients with AD than in age-matched controls and occur less often as disease progresses.

DLB is associated with abnormal control of consciousness throughout the day, with fluctuations in arousal and alertness. Patients with DLB have subcortical and cortical cholinergic deficits greater than those seen in AD and alteration in cholinergic activity may underlie the fluctuating level of consciousness observed in 80% of these patients (Byrne, 1989; Perry *et al*., 1998). Sleep in DLB has not been as extensively investigated as in AD, but abnormal control of motor function during sleep appears to be common. This may present as REM sleep behaviour disorder (RSBD), which is characterised by a loss of the muscle atonia normally seen in REM sleep and an 'acting out' of dreams (Schenk, 1997; Boeve *et al*., 1998). Normal REM sleep is characterised by muscle atonia particularly affecting the antigravity muscles and is initiated by cholinergic brainstem neurones. RSBD is more common in Parkinson's disease (*inter alia* Cornella *et al*., 1993, 1998), multiple system atrophy (Plazzi *et al*., 1997; Tachibana, 1997) and DLB (Boeve *et al*., 1998) than in age-matched controls. It is hypothesised that some sleep disturbance at night, especially the periodic limb movements, bad dreams and confusion on waking, are a result of REM sleep abnormalities. Detailed electro-physiological sleep work has yet to be done in DLB, but the more profound cholinergic deficits seen could be predicted to cause extensive disruption to sleep architecture, particularly REM related phenomena.

Although changes in 24-hour arousal are common in both AD and DLB and are clinically important, physiological measures of sleep profile such as EEG polysomnography are time consuming, expensive and limited to a few centres. In this paper sleep questionnaires are used to quantify the previously documented sleep disorders in groups of patients with AD and DLB. Measurements were made of night-time behaviour disturbance, daytime sleepiness and carer distress.

A small subset of the DLB patients were enrolled in an open label study of rivastigmine, a cholinesterase inhibitor, enabling a pilot study of the effects of this class of drugs on sleep/wake cycles.

METHOD

Patients were recruited from a specialist centre in old age psychiatry, either from day hospital contact or memory clinic assessments. Patients were recruited consecutively after initial assessment by the clinical team. All patients with a possible diagnosis of AD or DLB were screened for possible inclusion in the study. If they met the recently agreed consensus criteria for DLB (McKeith *et al*., 1996) or National Institute of Neurological and Communicative Disorders and Stroke (NINCDS) (McKhann 1984) criteria for probable AD and had a carer able to give a sleep history, they were approached to take part in the study. Patients with a recorded diagnosis of depression or chronic pain were excluded from this study as they may be predicted to have altered sleep patterns.

For each subject, the Mini State Examination (MMSE; Folstein *et al*., 1975) was used to provide a simple global measure of cognitive functioning and CDR (clinical dementia rating scale) was used to stage the degree of global severity. Details of night-time medication were recorded.

The sleep scales used were the Epworth Sleepiness Scale (ESS; Johns, 1993), which is an eight-item scale designed to quantify daytime sleepiness and tendency to 'nap' by rating the likelihood of falling asleep in different situations on a scale of 'never' to 'highly likely', scoring 0–3 for each time, giving a range of 0–24. The Pittsburgh Sleep Quality Inventory (PSQI; Buysee *et al*., 1988) is a seven-component scale designed to measure sleep disturbance over the preceding month. Each component has a value on the scale of 0 (no sleep disturbance) to 3 (high level of sleep disturbance), giving a ratio of 0–21. It has been validated in nursing home populations (Gentili *et al*., 1995). The carer distress scale from the sleep item of the Neuropsychiatric Inventory (NPI; Cummings *et al*., 1994) was used, rating distress over the preceding 4 weeks on a six-point scale from 0 to 6 ('not a problem' to 'very severe problem').

For the patients on rivastigmine, all the rating scales were repeated after 12 weeks of treatment on maximum tolerated dose.

RESULTS

Seventeen patients with DLB and 20 with AD were recruited from either day hospital care or community psychiatric nurse (CPN) contact. All were under the care of a psychogeriatrician. Six patients with DLB were started on rivastigmine and measures were repeated after 12 weeks' treatment at the maximum tolerated dose.

The AD and DLB groups were similar in terms of age, gender, and cognitive impairment, as measured by the MMSE, and level of global severity, as measured by CDR (Table 1). Six out of 20 (30%) of the AD patients and 5 out of 17 (29%) of the DLB patients were on hypnotic medication. More men than would be expected were recruited. This may be due to the exclusion of many female patients as they had no carer to provide a history.

Both groups demonstrated a tendency to fall asleep during the day, as measured by the ESS. The data show that the DLB group had a greater tendency to fall asleep at inappropriate times during the day. The DLB group also demonstrated more night-time sleep disturbance. Carers reported more distress at sleep disturbances in the DLB group than the AD group, with 16/17 saying that sleep problems were a stressor compared with 8/20 in the AD group (Table 2). A stressor was defined as a carer rating of moderate, severe or very severe on the six-point scale of the NPI.

In quantifying specific night-time sleep problems, DLB patients were more likely to demonstrate periodic limb movements, confusion on waking DLB, and bad dreams than the AD group. The scales used detected no significant difference between groups in subjective sleep quality, latency or duration (see Table 3).

In the small subgroup treated with rivastigmine at maximum tolerated dose there was a reduction in both ESS and PSQI scores and reduced incidence of individual troublesome night-time behaviours, such as bad dreams, periodic limb movements and confusion on waking (Table 4). None of these patients were on hypnotic medication. Due to the small numbers, statistical analysis was not carried out.

DISCUSSION

The three questionnaires used in this paper demonstrated a high incidence of sleep disturbance in both AD and DLB patients. Disturbances in the

Table 1. A comparison of baseline characteristics of the two groups

	Age mean (range)	Gender	MMSE mean (range)	CDR stage	Number on hypnotic medication
AD group, $n = 20$	74 (65–82)	14 male	18.0 (13–24)	0 at 0.5 16 at 1 4 at 2	6
DLB group, $n = 17$	74.9 (62–90)	13 male	15.6 (14–24)	1 at 0.5 11 at 1 5 at 2	5

Table 2. Sleep characteristics of AD and DLB patients

	ESS score mean (range)	PSQI score mean (range)	NPI carer distress score*
AD group, $n = 20$	6.5 (3–14)	4.6 (1–7)	8/20
DLB group, $n = 17$	12.6 (2–21)	8.5 (2–20)	16/17
	$t = 4.2$, $p = 0.01$	$t = 2.2$, $p = 0.04$	

* Moderate to very severe distress.

Table 3. Description of sleep characteristics

	AD group $n = 20$ (%)	DLB group $n = 17$ (%)	
Subjective sleep quality bad or fairly bad	3 (15%)	8 (53%)	NS
Sleep latency on average more than 30 min	3 (15%)	3 (18%)	NS
Sleep duration less than 6 hours per night	0	2 (12%)	NS
Sleep efficiency less than 75%	0	2 (12%)	NS
Limb movements*	2 (10%)	14 (82%)	$\chi^2 = 16.2$ $p = 0.02$
Confusion on waking	5 (25%)	17 (100%)	$\chi^2 = 19.8$ $p = 0.01$
Bad dreams*	7 (35%)	10 (58%)	$\chi^2 = 7.1$ $p = 0.05$

* Individual item on PSQI.

Table 4. Change in sleep characteristics after treatment

	MMSE mean (range)	ESS mean (range)	PSQI mean (range)	Periodic limb movement	Confusion on waking	Bad dreams	Carer burden
Pre-treatment, $n = 6$	18.5 (14–22)	14.7 (11–21)	8.8 (8–10)	5/6	6/6	4/6	6/6
Post-treatment, $n = 6$	23.0 (16–26)	8.0 (5–11)	4.7 (3–7)	3/6	4/6	2/6	4/6

control of wakefulness and sleep are apparent in both groups. DLB patients had higher levels of sleep disturbance overall and specifically had more abnormalities in areas such as control of movement (periodic limb movements), bad dreams and confusion on waking. These findings imply that the ESS and PSQI detect some of the differences in sleep profile previously documented using polysomnography.

The questionnaires used take approximately 15 minutes to administer and give a quantified measurement of sleep disturbances. Although the PSQI has been previously validated in nursing home populations, neither it nor the ESS are extensively used in psychiatric practice. Although the gold standard for the detection of sleep disturbance remains polysomnography (PSG) and daytime sleepiness can only be definitively assessed by intervention measures such as the multiple sleep latency test, whereby tendency to nap is monitored by an observer and EEG recording, the tools used in this study are brief and easily administered, showing a clear difference between the diagnostic groups and a possible improvement in sleep between treated and non-treated DLB patients.

A comparison of the ESS score between the groups shows a much greater tendency for the DLB group to sleep during the day. Fluctuations in consciousness are an integral part of the diagnosis of DLB and from the tools used it is difficult to separate fluctuation in arousal from sleep. The ESS, however, measures the tendency to fall asleep in a variety of situations, perhaps indicating a lower level of innate arousal in this patient group or reflecting the sleep deficit arising from a disturbed night's sleep.

The simple carer distress measure used indicates that the problems of sleep disturbance in both types of dementia are a significant cause of distress to carers. The low incidence of prescribed nighttime medication may represent a reluctance on the part of psychogeriatricians to prescribe addictive benzodiazepines or potentially dangerous neuroleptics, a lack of enquiry on the part of the treating doctor or previous ineffectual treatment with hypnotic medication. As discussed earlier, the typical change in sleep profile in AD and DLB is characterised by a loss of REM sleep and as most benzodiazepines and sedating antidepressants are REM suppressors, they may have a paradoxical effect on sleep. However, if sleep disturbances are related to REM abnormalities such as RSBD, REM sup-

KEY POINTS

- Patients with AD and DLB have high levels of sleep disturbance both during the day and at night.
- DLB patients have more sleep disturbance than AD patients with more confusion on waking and abnormal control of movement.
- Sleep questionnaires are sufficiently sensitive to discriminate between sleep patterns in AD and DLB and confirm the differences found by polysmonography.
- A small pilot study suggests that rivastigmine may correct some of the sleep disturbances seen in DLB.

pressing medication may have a beneficial effect on sleep architecture.

The early indications from the small number of patients started on rivastigmine are that there is a reduction in the level of sleep disturbance, with a fall in PSQI and a reduction in carer burden. (Six out of six reported an improvement in night-time behaviour.) Rivastigmine also reduced daytime sleepiness, as reflected in the fall in ESS, perhaps demonstrating the role of the cholinergic system in the control of arousal. If larger trials show an improvement in sleep profile with the prescription of cholinesterase inhibitors for the treatment of cognitive impairment or non-cognitive symptoms of dementia, the need for more potentially dangerous drugs such as benzodiazepines or neuroleptics may be reduced.

CONCLUSIONS

Distressing night-time behaviours and daytime sleepiness are common in AD and DLB, but are more common in DLB. Few patients are on hypnotic medication. The scales used in this study are sensitive enough to detect the differences between AD and DLB patients, confirming the differences seen in polysomnography studies. Disruptions in night-time behaviour and excessive daytime sleepiness may respond to rivastigmine.

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